

## **REMARKS**

Claims 1-3, 5, 10, 11, 13, 14, and 21-36 are currently presented to the Examiner. No claims have been amended, added or canceled with this response. Applicant provided the claims above for the Examiner's convenience. Further, Applicant submits herewith a Supplemental Declaration of Dr. Vassilios Papadopoulos Under 37 C.F.R. §1.132 in Support of Patentability.

### **I. Rejection Under 35 U.S.C. § 103**

Claims 1-3, 5, 10, 11, 13, 14, and 21-36 were rejected under 35 U.S.C. §103 as being unpatentable over Devita et al. in combination with Beale and Lemay et al. Applicant respectfully traverses the rejection and requests withdrawal of the same.

The Examiner argues that he has presented a *prima facie* case of obviousness and therefore the burden to rebut the *prima facie* case is on the Applicant. Applicant respectfully submits, however, that the Examiner has not set out a *prima facie* case for obviousness because: (1) the prior art references, neither alone or in combination, teach the recitations of the Applicant's claims; and (2) even if the combination of prior art references did teach the claimed invention, there was no motivation to combine the references. Further, even if a *prima facie* case has been established, which Applicant contends has not, Applicant has sufficiently rebutted the Examiner's arguments with a showing of unexpected results achieved by the claimed invention.

#### ***a. The Elements of Claims 1-3, 5, 10, 11, 13, 14, and 21-36 are not Disclosed in the Prior Art***

Contrary to the Examiner's assertions that Claim 1 claims "a composition comprising at least two anti-HIV drugs and a cortisol blocker," Claim 1 recites a pharmaceutical composition for enteral administration comprising at least one anti-HIV drug and a cortisol blocker comprising procaine HCl, zinc heptahydrate, and ascorbic acid.

Claims 2-3, 5, and 21-28 depend from independent Claim 1. Therefore, the patentability of Claim 1 over the prior art establishes the patentability of Claims 2-3, 5, and 21-28.

Claim 10 recites, among other things, a method for the treatment of HIV infected patients comprising enterally administering to the patient at least one anti-HIV drug and a cortisol blocker comprising procaine HCl, zinc heptahydrate, and ascorbic acid.

Claims 11, 13, 14, and 29-36 depend from independent Claim 10. Therefore, the patentability of Claim 10 over the prior art establishes the patentability of Claims 11, 13, 14, and 29-36 over the prior art.

Devita et al. allegedly discloses that combinations of *anti-HIV drugs* are beneficial in treating HIV infection. There is no mention of a cortisol blocker utilized in combination therapy.

Beale allegedly teaches the use of anti-cortisol compounds such as HMB, DHEA, Ipriflavone and phosphatidylserine in the treatment of patients with AIDS to reduce the catabolic effects associated with AIDS. Beale does not teach the use of anti-cortisol compounds in a composition with anti-HIV drugs. Further, the compounds that Beale characterizes as cortisol blockers may or may not affect muscle catabolism in a manner unrelated to cortisol levels.

LeMay et al. do not teach that the cortisol blocker ketoconazole in combination with zidovudine (AZT) can be used for HIV therapy. LeMay et al. teach that, in the case where HIV-infected infants present mucocutaneous candidasis, then one could treat them with ketoconazole, a safe and effective therapy of candidasis. The goal of the Lemay et al. study was to assess the use and safety of a ketoconazole and zidovudine combination therapy to infants.

None of the cited references, alone or in combination, teach the combination composition as recited in Claim 1. Particularly, the cited references do not teach or suggest a cortisol blocker

mixture including procaine HCl, zinc heptahydrate, and ascorbic acid. Applicant respectfully submits that Claim 1 is patentable over the cited art.

None of the cited references, alone or in combination, teach the method of treating an HIV infected patient as recited in Claim 10. Particularly, the cited references do not teach or suggest administering to a patient a cortisol blocker mixture including procaine HCl, zinc heptahydrate, and ascorbic acid. Applicant respectfully submits that Claim 10 is patentable over the cited art.

It is well established that the burden of establishing a *prima facie* case of obviousness lies with the Examiner. In determining obviousness, one must focus on the invention as a whole.

*Symbol Technologies Inc. v. Opticon Inc.*, 19 USPQ 2d 1241, 1246 (Fed. Cir. 1991). The primary inquiry is: “Whether the prior art would have suggested to one of ordinary skill in the art that this process should be carried out and would have had a reasonable likelihood of success....

Both the suggestion and the expectation of success must be found in the prior art, not the applicant’s disclosure.” *In re Dow Chemical*, 5 USPQ 2d 1531 (Fed. Cir. 1988). When all the prior art is considered together, a person having ordinary skill in the art must have a sufficient basis for the necessary predictability of success to sustain a rejection under 35 U.S.C § 103. See *Ex parte Novitski* 26 USPQ2d 1389 (Bd.Pat.App. & Int. 1993), citing *In re Clinton*, 188 USPQ 365 (CCPA 1976).

The cited references do not teach or suggest to one of ordinary skill in the art the present claimed invention, particularly the presently claimed cortisol blocker mixture including procaine HCl, zinc heptahydrate, and ascorbic acid. There is no teaching or suggestion that the combination of procaine HCl, zinc heptahydrate, and ascorbic acid would produce a greater anti-cortisol effect than any of the components taken alone. Thus, these references do not provide

one of ordinary skill in the art that the present claimed invention would have had a reasonable likelihood of success.

Again, both the suggestion and the expectation of success must be found in the prior art, not the applicant's disclosure. From the cited references, a person having ordinary skill in the art would not have a sufficient basis for the necessary predictability of success to sustain a rejection under 35 U.S.C § 103.

*b. No Motivation to Combine*

None of the references suggest combining an anti-HIV drug with procaine HCl, zinc heptahydrate, and ascorbic acid as recited in the claims. For example, Beale teaches away from the use of compounds such as ketoconazole disclosed in Lemay et al. As discussed above, Lemay et al. teach the use of ketoconazole to treat HIV-infected infants with mucocutaneous candidasis. Ketoconazole is a general steroidogenic enzyme cytochrome P450 inhibitor, which blocks the synthesis of androgens and estrogens. Due to the effects on androgen synthesis, ketoconazole should not be used in long term HIV therapy. Inhibition of androgen synthesis will ultimately lead to increased catabolism and thus to reduced body mass, a major issue in HIV. One of skill in the art would therefore not have the motivation to combine Lemay et al. with Beale because Beale teaches the use of his alleged anti-cortisol to reduce catabolism.

None of the cited references, alone or in combination, provide the motivation to combine a cortisol blocker mixture including procaine HCl, zinc heptahydrate, and ascorbic acid with an anti-HIV drug as recited in the claims. Applicant respectfully submits that the pending claims are patentable over the cited art.

*c. Applicant's §1.132 Declaration Reveals Unexpected Results Achieved by the Claimed Invention*

The accompanying §1.132 Declaration of Dr. Vassilios Papadopoulos of Georgetown University reveals a synergistic anti-cortisol effect obtained from the combination of procaine HCl, zinc heptahydrate, and ascorbic acid. The anti-cortisol effect of the combination of drugs was extremely elevated in comparison with the anti-cortisol capabilities of each ingredient taken separately. Exhibit A of Dr. Papdopoulos's Declaration provides results from the study discussed in Dr. Papdopoulos's September 18, 2000 Declaration. Applicant respectfully submits that these results evidence that the claimed invention achieves unexpected results, thereby rebutting the Examiner's alleged *prima facie* case of obviousness.

**II. Conclusion**

With entry of the above Amendment and in view of the foregoing remarks, it is respectfully submitted that claims 1-3, 5, 10, 11, 13, 14, and 21-36 are in condition for allowance.

None of Applicant's amendments or cancellations are to be construed as dedicating any such subject matter to the public, and Applicant reserves all rights to pursue any such subject matter in this or a related patent application.

It is respectfully submitted in view of the foregoing Amendment and Remarks that all of the objections and rejections in the Office Action dated March 6, 2003 have been overcome and should be withdrawn. Applicant respectfully requests early and favorable notification to that effect. The Examiner is encouraged to contact the undersigned with any questions or to otherwise expedite prosecution.

Respectfully submitted,

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